ISSN 0918-8959

continuation of
ENDOCRINOLOGIA JAPONICA

Endocrine Journal

The 8th Meeting of the Immunology of Diabetes Society (IDS-8)

Program & Abstracts

THE JAPAN ENDOCRINE SOCIETY
SINCE 1925

Vol.52 Suppl.
October 2005

PUBLISHED BIMONTHLY BY The JAPAN ENDOCRINE SOCIETY
http://square.umin.ac.jp/endocrine

P-110

A POSSIBLE IMPLICATION OF SOLUBLE CTLA-4 IN TYPE 1 DIABETES

***Nyholm J-C, *Rigolio R, * Zaigham I.H., #Ivarsson S., and Cilio C.M.*#**
***Cellular Autoimmunity Unit, Dept. of Clinical Sciences and #Dept. of Pediatrics, Malmö University Hospital, Malmö, Sweden**

Background/Rational: Type 1 diabetes is a polygenic organ-specific autoimmune disease caused by the destruction of insulin-producing β-cells in the pancreas. Genetic linkage and association studies have suggested *CTLA4* as a candidate gene for the diabetes susceptibility locus *IDDM12*. Although the genetic association has been confirmed several times, a biological defect of CTLA-4 expression and/or function in T1D patients has not been demonstrated to date. CTLA-4 is a surface receptor expressed on T cells upon activation and which is constitutively expressed on regulatory T cells. While CTLA-4 is a negative regulator of T cell reactivity, the role of this molecule in the function of regulatory T cells is still elusive. Alternative mRNA spliced form of *CTLA4*, coding for a shorter soluble protein (ligand-binding) (sCTLA-4) but lacking the trans-membrane domain, exist in human, mouse and rat and it has been shown to be decreased in individuals carrying the disease-associated haplotype of *CTLA4*. Higher levels of sCTLA4 have been previously demonstrated in other autoimmune diseases like thyroiditis and LES as well as in asthma.
Aim: The aim of this pilot study was to investigate serum levels of sCTLA-4 in patients affected by T1D (n=14) compared with healthy individuals (n=22) and patients with thyroiditis (ATD) (n=24).
Methods: Serum sCTLA-4 levels were measured using a commercially available ELISA kit following the manufacturer recommendations.
Results: Surprisingly, we found higher levels of serum sCTLA-4 in T1D patients compared to healthy controls, (mean 1,84±1,14 ng/ml vs. 0,16± 0,84 ng/ml, respectively. p=0,005) and we confirmed the increased levels in ATD.
Conclusions: These preliminary results reinforce a possible role for CTLA-4 in T1D and ATD. We speculate that the sCTLA-4 binding to B7 surface receptors on dendritic cells may interfere with inhibition of pathogenic self-reactive T cells or with the suppressive function of regulatory cells. Larger studies using high throughput technology and correlation with susceptibility *CTLA4* genotypes together with functional studies are underway to clarify the biological significance of these results.